Author’s response to reviews

Title: MULTISITE MUSCULOSKELETAL PAIN IN MIGRANTS FROM THE INDIAN SUBCONTINENT TO THE UK: A CROSS-SECTIONAL SURVEY

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Author’s response to reviews:

We thank the reviewers for the time and effort that they have put into reviewing our paper, which we have revised substantially, including a new figure and tables. As requested by the journal, we have removed the tracking of changes from the manuscript. In addition to the changes in response to reviewers’ comments (see below), we have:

• Added clarification in the funding section that none of the funders had any role in the design of the study, the collection, analysis or interpretation of data, or writing the manuscript.

• Included a statement in the Authors’ Contributions section indicating that all authors have read and approved this latest version of the manuscript.

• Clarified what was covered by the ethical approval

• Uploaded English language versions of the questionnaires that were used.

Reviewer:

Therese Nordberg Hanvold: Review of PMSD-D-18-001171R1: Multisite musculoskeletal pain in migrants from the ….
The authors use data from a cross-sectional survey to study the prevalence of multisite pain among Indian workers, white UK workers and UK immigrant workers from India. They found differences in pain showing a significantly lower prevalence among Indian workers in India compared to the white UK workers and UK immigrant workers from India. The issue of international variation in the prevalence of musculoskeletal pain is an important topic to address. The attempt to disentangle the effect of the work exposure, the individual characteristics and the cultural influence is complex and challenging, but highly valuable. The study results add to the knowledge of international variation in pain. However, the manuscripts have substantial scientific shortcomings. In the presentation of background and a lack of a clear hypothesis. Information on validated methods is missing, the analyses seem to lack a power and the discussion lack references beyond the CUPID study. There is also some conclusions drawn from the manuscript that the results in the manuscript do not suggest. There is also long and difficult sentences throw-out the manuscript that seems unfinished, proofreading is essential. Please find my major comments below.

RESPONSE

As with all research, epidemiological studies should address defined questions. However, they do not have to test hypotheses. Our three study questions are set out in penultimate paragraph of the Background. We have modified and expanded the wording to make them more explicit.

We have added further information about the methods that we used (see below).

We believe that our analyses have adequate power, and support the conclusions that we draw. We have expanded the Results and Discussion to make this clearer (see below).

The reviewer does not identify any specific examples of long and difficult sentences in the file that was attached. However, we have broken up two longer sentences in a way that we hope will make the paper easier for readers whose first language is not English.

1. The Background section lacks a clear presentation and understanding of why the “first step“ to understanding the unidentified causes of pain at multiple anatomical sites is to know if the prevalence is different between Indian workers, immigrant UK workers from India and white UK
The aim presented is also quite ambiguous and I do not think the data or the analysis are able to answer these questions.

RESPONSE

Importantly, our wording is “a first step”, not “the first step”. We do not claim that our approach is the only possible way forward at this stage. Nor do we suggest that it is important to know whether the prevalence of musculoskeletal pain differs between Indian workers and white UK workers. Before we began our study, we already knew that within our study sample, the prevalence of pain at specific anatomical sites was much lower in Indian than UK white workers. That is why we chose to address our study questions using that study sample.

The three questions that we aimed to address are those set out in the penultimate paragraph of the Background, and concern what happens in migrants from the Indian subcontinent to the UK. We remain of the view that they offer a useful way of narrowing the search for the factors that drive the apparently wide international variation in general propensity to musculoskeletal pain that we have demonstrated previously in the CUPID study.

We have expanded the penultimate paragraph of the Background to make more explicit why it would be helpful to answer the three stated study questions. We have also reviewed the wording of those questions, and discussed it with colleagues, and we cannot understand in what way they are considered ambiguous. We have added clarification at the end of the Background that within our chosen study sample, it had already been shown that rates of pain in the back, neck and arm were much lower in Indian manual workers than among manual and non-manual workers in the UK, and that office workers in India had lower rates of pain in the wrist and hand than office workers in the UK, although the occurrence of pain at multiple anatomical sites in the same individuals had not been examined.

As we argue in the responses that follow, we believe that the analyses presented do help to answer our three study questions. We accept the reviewer’s point that power was more limited in the subsidiary analyses that were restricted to participants aged 17-34 years (we have now added 95%CIs to the text to make the power clearer) and first generation migrants. Nevertheless, the pattern of results is similar to that in the main analysis, and we have now added a number of direct pairwise comparisons of risk between the various groups of workers, which suggest that the observed differences between Indian workers and workers in the UK (including those of Indian subcontinental origin) are unlikely to have arisen from random sampling
variation. We also have added a paragraph to the Discussion to make this clearer, and modified our wording to acknowledge the more limited power of the subsidiary analyses.

I propose that the authors adjust the aim adjusted to the data they have available: to address if there is international variation in the prevalence of musculoskeletal pain between white UK workers and Indian workers. Secondly how UK immigrant workers from India resembles in terms of msd.

RESPONSE

We appreciate the reviewer’s suggestion, but we see little value in taking as our study question whether there is international variation in the prevalence of musculoskeletal pain between white UK workers and Indian workers. We already know from the CUPID study that among working populations, rates of disabling musculoskeletal pain are substantially higher in the UK than in the Indian subcontinent (Pakistan and Sri Lanka) [1-2]. Moreover, earlier analysis of the dataset used for the current paper demonstrated that rates of pain in the back, neck and arm were much lower in Indian manual workers than among manual and non-manual workers in the UK [3]. Also, office workers in India had lower rates of pain in the wrist and hand than office workers in the UK [3]. As mentioned above, we have now added this information to the last paragraph of the Background, to make the rationale for the study design clearer.

2. The Methods section refers to reference 5 in terms of methods of data. This is ok to some extent, but the manuscript should give some information on the most relevant outcomes and exposure used in the analysis. The method section lacks information on the methods used to collect data in terms of musculoskeletal pain. Was it a validated questionnaire used? Was there any information on the intensity or frequency of pain? Was there a mannequin/drawing indicating the body areas in pain to help the participants indicating for example where the neck and shoulder starts and ends? Information on how work exposures was asses is also missing. The only reference is to the SF36 and no information of the distribution is given so that the grading into three levels is impossible to interpret. The UK immigrant workers from India also lack a definition (such as info on how long have they been in UK)

I propose that the authors gives clear descriptions on how all the variables in the 1 and 2 was assessed and grouped using references.
RESPONSE

We had tried to make our report concise, but we agree that further detail of our methods could be helpful for many readers, and we have now added it as requested.

Of the variables listed in Table 1, age and sex are straightforward, and should not require amplification. We already explain that mental health was assessed using items derived from the SF-36 questionnaire (with exclusion of one question that could not be translated satisfactorily), and that scores were graded to three levels (good, intermediate or poor) corresponding to approximate thirds of the overall distribution. To make this clearer, we have added “of scores in all subjects (i.e. with cut-points at approximate tertiles)”. We have redrafted, and slightly expanded our description of how physical activities at work were assessed. And we have added a new paragraph describing in detail how psychosocial exposures were defined.

We have added a further new paragraph explaining that the questions on pain were adapted from the Nordic questionnaire (giving a reference), and that we used diagrams to illustrate the relevant parts of the body. We are uncertain what the reviewer means when she asks whether the questions about pain were “validated”. Pain is a subjective symptom, and there is no gold standard against which the accuracy of its report can be assessed. Moreover, it can fluctuate over time, so a lack of repeatability in its report does not necessarily imply a lack of validity. Perhaps most helpful is whether the questions about pain have predictive validity. We have found that near identical questions used in the CUPID study had predictive validity for subsequent report (more than a year later) of pain at other anatomical sites [4 and submitted for publication] and for associated sickness absence [submitted for publication]. We did also ask about duration of pain in the past year, and whether it had led to medical consultation, sickness absence or disability for specified activities of daily living. However, we did not use those data in the analysis for the current paper. One reason was that access to medical consultation and propensity to take sickness absence may vary between countries and jobs for reasons other than the severity of pain.

Another new paragraph describes how ethnic origin was ascertained, and how first and later generations of migrants to the UK were distinguished. We did not ask how long migrants had been in the UK, but our expectation is that those who described themselves as second or more generation would have been born in the country.

3. The Results section is presented in nice tables and figures. However, the definition of multisite pain is presented as ≥2, ≥3 and ≥4 pain areas in Table 3. Looking at table 2, it is clear that one
might have ≥2 but this is really only in the shoulders (right/left). This illustrated the importance of defining what multisite pain is and have a clear understanding on the hypothesis. In Table 4, it is also evident that there is a lack of power in the analysis for pain sites ≥3 and ≥4 especially in the Indian workers when adjusting for all the variables in table 1. There is only six and four Indian manual workers in the ≥3 and ≥4 pain analysis and you are adjusting for many covariates.

I propose that the authors defines multisite pain and maybe group shoulder pain together and wrist pain together to highlight the pain at different anatomical sites. I also suggest that the analysis is done to analyses the international variation in pain and maybe not multisite pain, as there is a lack of power to do this for these data.

RESPONSE

In preparing copies of the original questionnaires for uploading to the journal’s website, we discovered that the questionnaire which was used to collect data in India, unlike that used in the UK, did not ask about the laterality of pain in the elbow or wrist/hand (only the shoulder). As a consequence, the coding of pain at those two sites for the two groups of workers in India had been misinterpreted, and the number of sites with pain undercounted for members of those groups who had bilateral pain in either the elbow or wrist/hand. To address this error, we have followed the reviewer’s suggestion, and have now grouped shoulder pain, elbow pain and wrist/hand pain as just three sites. However, because bilateral pain in the elbow and wrist/hand was uncommon, it makes little difference to the findings.

Table 3 now presents risk estimates for ≥1, ≥2, and ≥3 anatomical sites (from the total of five) with pain, and demonstrates that the patterns of risk across the six occupational groups are similar for each of these three nested outcomes. We did this to make clear that our conclusions did not depend critically on our preferred definition of multisite pain (pain at ≥3 anatomical sites), and we think that the information may be helpful to readers.

The reviewer has misinterpreted the numbers of participants included in the analyses. The analyses for ≥3 sites of pain in Indian manual workers included 107 workers with no pain as well as the 6 with pain at ≥3 sites. When comparing prevalence rates, statistical power depends not only on the numerators of the rates, but also the denominators. For example, if an outcome occurred in 500 out of 1000 people in one sample and 2 out 1000 in another, the difference in
prevalence would be highly significant statistically, even though the second prevalence was based on only two cases.

The 95% CIs around the risk estimates provide a better guide to power. In the text, we have now added odds ratios and 95% CIs for direct comparisons of Indian manual workers with the two groups of UK workers of Indian subcontinental origin, confirming that in both cases, the differences were unlikely to have resulted from random sampling variation.

The reviewer is correct that the adjustment for multiple covariates leads to greater statistical uncertainty, and that is reflected in the wider confidence intervals for risk estimates after adjustment. However, as indicated above, the differences between occupational groups in the fully adjusted analyses were statistically significant.

The subsidiary analyses are based on smaller numbers, and therefore have less statistical power. Nevertheless, the confidence intervals around risk estimates again indicate that the differences in prevalence from Indian manual workers are unlikely to have occurred by chance, and the overall pattern of results is similar to that in the main analyses. We have added extra information about confidence intervals in the last paragraph of the Results, and a new paragraph in the Discussion which considers the potential for random sampling error.

4. The Discussion section has several good reflections, however it lacks references beyond the CUPID study and some reflection on limitations because of the study size, methods etc. Overall, the discussion should be rewritten in terms of the earlier comments.

RESPONSE

Quite a few studies have assessed the prevalence of multisite pain in different ethnic groups, but because of differences in the study populations (general vs. employed, age ranges) and the specification of pain outcomes (number and distribution of anatomical sites affected, for how long, and over what period), their results cannot be closely compared with ours. We have added a new sentence to what is now paragraph 8 of the Discussion to make this point.
We have still been unable to identify any published reports that have used standardised methods to compare the prevalence of musculoskeletal pain in migrant populations with those both in their region of origin and in the country to which they have moved. However, we have now added a new paragraph to the Discussion referring to three studies which have compared pain prevalence (by various definitions) in UK populations of white European and South Asian origin.

The limitations of the study, and their potential implications for interpretation, are discussed in paragraphs 2 to 6 of the Discussion. Specifically, we considered the possibilities of: confounding by differences in physical demands of work; bias from healthy worker selection; bias from errors in recall; missing information on the laterality of pain, and differences in understanding of the term, pain. To this, we have now added a further paragraph discussing the power of our analyses and potential for random sampling error.

5. The Conclusion. The first sentence is possible to draw from the analysis and results, however I would be careful to say something about the start of the pain in life and that the impact start soon after people move to the UK. There is no scientific evidence in the manuscript to suggest this.

RESPONSE

We disagree with the reviewer’s assertion that there is no scientific evidence in the manuscript to suggest that whatever is responsible for the higher rates of pain in the UK starts to impact by early in adult life and soon after people move to the country. Although based on smaller numbers, our sub-analyses for younger participants and first generation migrants gave a pattern of results very similar to that for the full study sample. As reported in what is now the penultimate paragraph of the Results, among workers aged 17 to 34 years, in comparison with white non-manual workers in the UK, the prevalence of pain at ≥3 sites in Indian manual workers was much lower (fully adjusted OR 0.02, 95%CI 0.001-0.35), whereas that in UK non-manual workers of Indian subcontinental origin was no different (OR 1.15, 95%CI 0.39-3.43), and that in UK manual workers of Indian subcontinental only a little lower (OR 0.44 (95%CI 0.05-3.81). Furthermore, in first generation migrants to the UK, there was no indication that rates of pain were as low as those that we found among workers in India (ORs 1.80 and 0.80 for manual and non-manual workers in comparison to white non-manual workers) – see last paragraph of Results. To this we have now added confirmation that the differences from manual workers in India were statistically significant.
We accept, however, that the statistical power of these subsidiary analyses was more limited than that of the main analyses, and we have therefore modified the wording of our conclusion accordingly.

Subas Neupane (Reviewer 2): This is somewhat interesting manuscript that looked at the prevalence of multisite musculoskeletal pain among certain group of workers at the UK and India and those migrated to the UK from the Indian subcontinent. Author utilized data from a cross-sectional survey conducted among 814 participants. The authors found large differences in the prevalence of pain at multiple sites. In general the manuscript is nicely written. I have only few concerns which I hope could be helpful to improve the manuscript further.

The second part of the study aim, 'whether the change in multisite pain is apparent in the first generation migrants, and by what age it becomes manifest' is not very clear to me. I don't really convinced whether this aim is realized in their analysis. I can see that the authors have conducted a subsidiary analysis restricting the participants aged <35 years but it does not answer their research question presented above.

RESPONSE

With respect, we disagree. If as we have shown, the prevalence of pain is significantly higher among manual workers who are first generation migrants to the UK than among manual workers in India (last paragraph of results), it suggests that the change in multisite pain is apparent in first generation migrants, which is exactly the question that we posed. Similarly, if among participants aged <35 years, the prevalence of pain is significantly higher among manual workers who are first generation migrants to the UK than among manual workers in India (penultimate paragraph of Results), that is evidence that the change in prevalence of pain following migration is manifest by early in adult life.

There is a lot of earlier literature on multisite musculoskeletal pain on its prevalence and the associated factors both from the industrial and general population, however the author has covered very little in the background. At least some important and relevant study should be presented in the background.
RESPONSE

We agree that there is an extensive earlier literature on the prevalence and correlates of multisite musculoskeletal pain. However, most have focused on chronic widespread pain (defined in various ways), and are not directly relevant to the questions which we address in our study.

We have, however, added a new paragraph to our Discussion, referring to three other studies that have compared the prevalence of multisite pain (by various definitions) in UK populations of white European and South Asian origin.

In the methods, the authors should describe how musculoskeletal pain was measured in their survey?

RESPONSE

This is a good point. We have added further detail.

Also, it is unclear whether the survey in India and in the UK was conducted at the same time or different time of the year?

RESPONSE

It is unclear why this should be relevant. Regarding climate, seasons mean something very different in Mumbai as compared with the UK. Moreover, we are not aware of a literature to suggest that musculoskeletal pain is strongly seasonal in either country. And even if it were, the analysis focused on reports of pain in the past year, and not just at the time of completing the questionnaire.

The authors should also describe clearly how they measured/defined the first generation migrants from the Indian subcontinent to the UK.
RESPONSE

This is a helpful suggestion. We have now added the requested clarification.

Response to musculoskeletal pain is somewhat influenced by their culture and social environment. I agree with the explanation provided by the authors in the first sentence of the last paragraph of the discussion section about the awareness of musculoskeletal pain response to it. But I wonder, the prevalence of musculoskeletal pain in other low and middle income countries (LMICs) including India itself is high as shown in recent studies. I suggest that at least some comparison with the findings from other studies from India/other LMICs, and also the findings from ethnic minority studies should be compared and discussed briefly.

RESPONSE

The interest of our paper is not the prevalence of multisite pain in India per se, but what happens to the prevalence of such pain in migrants from the Indian subcontinent (which has relatively low, not high, rates of pain) to the UK (where rates are higher). We have been unable to find any other reports of multisite pain in India using case definitions similar to ours. And it is unclear how comparisons with other LMICs would be relevant to our study questions or conclusions. For what it's worth, the CUPID study found relatively high rates of musculoskeletal pain in LMICs in Central and South America, intermediate rates in Europe, Australia and New Zealand, and relatively low rates in Pakistan, Sri Lanka and Japan.

REFERENCES

